

YELLOW FEVER IN THE OLD WORLD.

BY

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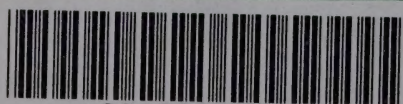
Professor of Tropical Medicine, University of Liverpool.

(Paper presented at a Meeting of the Society of Tropical Medicine
and Hygiene, Friday, June 16th, 1911).

[Reprinted from the TRANSACTIONS OF THE SOCIETY OF TROPICAL MEDICINE
AND HYGIENE, 1911, July. Volume IV. No. 8—pp. 233-237.]



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Ever since yellow fever was shown to be transmitted by *Stegomyia fasciata* the question has been before us as to why it is not as prevalent in the Old World as in the New. We have known for years that that mosquito is not only widely spread in the Eastern Hemisphere,* but is often very abundant in certain places. Moreover, the disease, or at least one which is clinically extremely like it, has been reported for centuries as occurring to some extent in West Africa, Spain and elsewhere—even at Swansea in England. We should therefore have thought that, as both the germ and the carrier were present in the Old World, the disease could have spread in it without difficulty.

Side issues of the same question have also been before us. Some years ago the fear was expressed that improved methods of ocean transit, and particularly the cutting of the Panama Canal, would, sooner or later, introduce the disease among the teeming populations of India and China; and quite recently there has been considerable discussion (especially at meetings of the Society of Tropical Medicine) of the suggestion that yellow fever not only occurs in West Africa, but (so far as I understand the proposition) abounds there to such an extent that it is endemic among the native population—rendering them immune and leaving the non-immune Europeans most open to infection. These are evidently different aspects of the general problem. If the disease abounds in West Africa, or even exists there, there is no immediately apparent reason why it should not have spread long ago, say, by way of Morocco and Algeria, into Egypt and thence to East Africa, India and China. From this point of view direct sea-carriage from America would not be necessary; endemicity in West Africa should have led to endemicity in every place where *S. fasciata* exists. Yet there are no grounds for supposing that it does exist, say, in Egypt, India and China. An acute disease with such a high case-mortality would have made its presence felt long ago among the non-immune Europeans in

* See, for instance, Mr. THEOBALD'S paper at the First International Congress of Entomology at Brussels.

those countries. Nothing like yellow fever as it used to prevail in Havana could have escaped attention, for example, in the large cities and garrisons of India. The precise question before us, therefore, is this one—can there be any factor which may suffice to prevent the spread of yellow fever in the Old World, in spite of the presence of *S. fasciata*?

I was not able to join in previous discussions on the subject because I wished to reserve my opinion until I had completed certain mathematical studies of epidemiology which I was then making; but the Society may now allow me to mention my results briefly without troubling them with the mathematical details. Clearly, epidemiology *must* be studied mathematically if it is to be studied accurately at all. It is not enough to say that an epidemic is due to a complex of factors. We must also try to ascertain how much each factor influences the result. This can be done only by mathematical treatment (which is merely ordinary reasoning rendered as precise as possible); and this is the only way in which we can ever hope to answer the question I have stated.

Yellow fever is one of the large class of metaxenous diseases—that is, diseases due to parasitic organisms which live in two species of hosts. The equations for the whole class are similar, but differ in detail for each disease because of difference in the constants—that is, the pathological phenomena, the immunity factors, the numbers, birth-rate, death-rate, immigration and emigration of both hosts, and the communicative factor (which is, in the case of yellow fever, the frequency of mosquito bites). The equations show the existence of three general laws: (1) The metaxenous disease will not continue to exist in a locality unless both the hosts are numerous enough; (2) A small increase of the numbers of one of these hosts above this point, which may be called the critical point, may cause a severe epidemic among the other species of host; (3) The disease will tend to reach a limit depending on the constants.

Applied to yellow fever the results can be stated very briefly. The mere presence of *S. fasciata*, even possibly in considerable numbers, may not be sufficient to maintain the disease anywhere. The insects must be numerous *enough*—must probably be, on the average, very numerous (the actual numbers required depends on the temperature, length of life, and other factors). To affect a large proportion of the human population, they must be comparatively extremely numerous.

As soon as this fact became clear I endeavoured to obtain evidence as to the comparative numerical prevalence of *S. fasciata* in various parts of the world. Scarcely any estimates were available; and indeed I suspect that even the records of local distribution are as often as not based rather on impressions than on entomological identifications—*S. sugens* and other species being quite possibly often lumped together with *S. fasciata*. In one case the statements made are statistically unreliable. I therefore wrote to Mr. F. V. Theobald, whose experience in the study of large collections from many parts of the world is of course very great, and whose authority on the subject is pre-eminent. He at once informed me that, judging from the huge collections which he has seen since 1899, he should say that *S. fasciata* is far more abundant in America and the West Indies than anywhere else. In India and Asia generally its place, he says, is almost entirely taken by *S. scutellaris*. In Africa it appears to be common only in a few districts; and in Europe it occurs only in small numbers in Italy, Spain, Greece, etc.

This evidence is probably as good as any that we shall ever obtain; and I therefore conclude that the absence of yellow fever in the greater part of the Old World is probably due to the comparative scarcity of the carrier.

It might also be due to a greater natural-immunity factor in Old-World varieties of *S. fasciata*; and I therefore asked Professor NEWSTEAD and Mr. CARTER of the Liverpool School of Tropical Medicine to see if they could detect any marked difference in specimens from the Eastern and Western Hemispheres. They could find none; and Mr. THEOBALD tells me that he does not think we can establish any such difference.

Another important point is elucidated by the equations. Hitherto it seems to have been generally held that, because both malaria and yellow fever are mosquito-borne, their epidemiology must be much the same. Now in malaria the parasites live in the human hosts often for long periods, but in the Anophelines, owing to the short life of the latter, only for a week or two (probably). In other words, in a malarious locality we shall find them at any given moment in a large proportion of the human beings, but only in a comparatively small proportion of the Anophelines; so that human beings, especially new comers (including children), form the reservoir of infection in malaria. But on working

out the yellow fever constants according to accepted observations, I was surprised to find that the proportion of infected persons (endemic ratio) must be extremely small in this disease, while the proportion of infected *Stegomyia* must be very large—just the opposite of malaria. In other words, even where yellow fever is endemic in a *place* it cannot be correctly said to be always or generally endemic among the *human population*. It must be the *mosquitoes* and not the men which are the principal reservoirs of the yellow fever virus. And this must be apparent after a moment's consideration, without mathematical computation. Yellow fever is an acute disease with rapid case-immunity; and as shown both by man-to-man and mosquito-to-man inoculations, ceases to be infective in about three days after the commencement of the illness. Thus, except perhaps shortly after the commencement of a severe epidemic among *non-immunes*, all the human material is, so to speak, so rapidly used up that few infected persons will be found on any one day, even in a very large population. At the same time, unless the *Stegomyia* supply and the communicative factor are maintained at a very high level, the epidemic may cease with great rapidity. This explains—if the fundamental observations are sound—why yellow fever is principally a disease of large crowded populations with a high *Stegomyia* index, such as Havana was; and we must not for a moment assume that phenomena similar to those found there and in other American cities must necessarily occur also in other parts of the world, even though *S. fasciata* is present, or even abundant.

The phenomenon of a *smouldering* metaxenous disease is due to the presence of one of the hosts in numbers which average just a little above the critical point. These hosts will of course not be uniformly distributed—they will be below the critical point at some spots and above it at others. Thus the disease will occur, so to speak, *in pockets*—will die out completely over large areas and will be just able to maintain a footing in particularly favourable ones, and perhaps to break out in small epidemics during specially favourable seasons. Yellow fever in West Africa comes most probably under this heading, and we must not assume without clear proof, because scattered cases may be detected there, that the whole native population is affected and immunised as in Havana. The case appears to be analogous to that of other diseases, such as that of bilharziasis—which is widely endemic in East Africa, but can only just keep a footing on the west coast of India.

Yellow fever belongs to a group of non-malarial insect-borne diseases—dengue, sandfly-fever, and probably others—the diagnosis of which is often very difficult unless autopsies and microscopical methods are generally used, and unless a marked epidemic is in progress. Hence in “smouldering diseases,” where epidemics are slight and rare, diagnosis is so far from easy that numbers of the cases may be returned, even to-day, under almost any heading which happens to be the fashion of the moment—and what must have been done years ago? For example, a case of suspected yellow fever in a ship just returned from Brazil was admitted into hospital under me a few weeks ago in Liverpool. There was high fever which had recently commenced; flushed face, rather slow pulse, and marked albuminuria. No typhoid or paratyphoid reactions followed and no organic mischief was discovered. Yet the temperature took three weeks to fall (by lysis), and a single *Plasmodium vivax* was found on the twenty-second day after admission! Numbers of equally indefinite cases occur in all tropical practice and are classed by the clinician as he pleases. Yet there can be absolutely nothing approaching scientific proof as to their true nature.

I conclude then that the most probable reason why yellow fever has not been able to spread in the Old World is simply that, for some unknown cause, *Stegomyia fasciata* is not so abundant in it as in the New World.

